<u>In the Specification;</u>

On page 8, please replace the paragraph beginning on line 27 with the following:

Figures 1A-B depict[[s]] the cDNA sequence and predicted amino acid sequence of human CARK. The nucleotide sequence corresponds to nucleic acids 1 to 3025 of SEQ ID NO:1. The amino acid sequence corresponds to amino acids 1 to 835 of SEQ ID NO: 2. The coding region without the 5' and 3' untranslated regions of the human CARK gene is shown in SEQ ID NO:3.

On pages 8 and 9, please replace the paragraphs beginning on line 34 of page 8 with the following:

Figures 3A-L depict[[s]] an alignment of the CARK protein with the A. Thaliana kinase 2 (Accession No.Z97337), A. Thaliana kinase 3 (Accession No. AC003113), Arabidopsis thaliana (Accession No. AL031135), C. elegans kinase (Accession No. AF024491), D. discoideum protein tyrosine kinase (Accession No. A35670), D. discoideum protein tyrosine kinase (Accession No. U01064), H. sapiens serine/threonine kinase (Accession No. Z48615), human raf1 (Accession No. W13107), human Raf1 kinase (Accession No. R98215), and soybean kinase (Accession No. M67449) using the Clustal method with a PAM250 residue weight table.

Figures 4A-B depict[[s]] the results of a search which was performed against the HMM database in which ankyrin repeat domains and a protein kinase domain were identified in the human CARK protein.

Figures 5A-D depict[[s]] the cDNA sequence and predicted amino acid sequence of rat CARK. The nucleotide sequence corresponds to nucleic acids 1 to 3026 of SEQ ID NO:7. The amino acid sequence corresponds to amino acids 1 to 835 of SEQ ID NO: 8. The coding region without the 5' and 3' untranslated regions of the rat CARK gene is shown in SEQ ID NO:9.

Figures 6A-B depict[[s]] the results of a search which was performed against the HMM database in which ankyrin repeat domains and a protein kinase domain were identified in the rat CARK protein.

Figures 7A-F depict[[s]] a global alignment of the human CARK nucleic acid sequence with the rat CARK nucleic acid sequence using the GAP program in the GCG software package, using a nwsgapdna matrix a gap weight of 12 and a length weight of 4. The results showed a 82.2% identity between the two sequences.

Figures 8A-B depict[[s]] a global alignment of the human CARK protein with the rat CARK protein using the GAP program in the GCG software package, using a Blosum 62 matrix and a gap weight of 12 and a length weight of 4. The results showed a 91.4% identity between the two sequences.

On pages 13 and 14, please replace the paragraph beginning on line 20 of page 13 with the following:

To identify the presence of an ankyrin repeat domain in a CARK protein, and make the determination that a protein of interest has a particular profile, the amino acid sequence of the protein is searched against a database of HMMs (*e.g.*, the Pfam database, release 2.1) using the default parameters (www.sanger.ac.uk/Software/Pfam/HMM_search). For example, the hmmsf program, which is available as part of the HMMER package of search programs, is a family specific default program for MILPAT0063 and a score of 15 is the default threshold score for determining a hit. Alternatively, the threshold score for determining a hit can be lowered (*e.g.*, to 8 bits). A description of the Pfam database can be found in Sonhammer *et al.* (1997) *Proteins* 28(3)405-420 and a detailed description of HMMs can be found, for example, in Gribskov *et al.*(1990) *Meth. Enzymol.* 183:146-159; Gribskov *et al.*(1987) *Proc. Natl. Acad. Sci. USA* 84:4355-4358; Krogh *et al.*(1994) *J. Mol. Biol.* 235:1501-1531; and Stultz *et al.*(1993) *Protein Sci.* 2:305-314, the contents of which are incorporated herein by reference. A search was performed against the HMM database resulting in the identification of nine ankyrin repeat domains in the amino acid sequence of human CARK (SEQ ID NO:2) at about residues 66-99, 100-132, 133-165, 168-198, 199-233, 234-268, 269-302, 306-338, and 339-371 of SEQ ID NO:2. The results of the search are set forth in Figures 4A-B. Nine ankyrin repeat domains were also identified in the amino acid sequence of rat CARK (SEQ ID NO:8) at about residues 66-99, 100-132, 133-165, 168-198, 199-233, 234-264, 269-302, 306-338, and 339-371 of SEQ ID NO:8. The results of the search are set forth in Figures 6A-B.

On page 14, please replace the paragraph beginning on line 20 with the following:

To identify the presence of a protein kinase domain in a CARK protein, and make the determination that a protein of interest has a particular profile, the amino acid sequence of the protein is searched against a database of HMMs as described above. A search was performed against the HMM database resulting in the identification of a protein kinase domain in the amino acid sequence of human CARK (SEQ ID NO:2) at about residues 463-716 of SEQ ID NO:2. The results of the search are set forth in Figures 4A-B. A protein kinase domain was also identified in the amino acid sequence of rat CARK (SEQ ID NO:8) at about residues 463-716 of SEQ ID NO:8. The results of the search are set forth in Figures 6A-B.

On page 16, please replace the paragraph beginning on line 19 with the following:

The nucleotide sequence of the isolated human CARK cDNA and the predicted amino acid sequence of the human CARK polypeptide are shown in Figures 1A-B and in SEQ ID NOs:1 and 2, respectively. A plasmid containing the nucleotide sequence encoding human CARK was deposited with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209, on March 21, 2000 and assigned Accession Number PTA-1530. This deposit will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an admission that a deposit is required under 35 U.S.C. §112.

On pages 16 and 17, please replace the paragraph beginning on line 31 of page 16 with the following:

The nucleotide sequence of the isolated rat CARK cDNA and the predicted amino acid sequence of the rat CARK polypeptide are shown in Figures 5A-D and in SEQ ID NOs:7 and 8, respectively. A plasmid containing the nucleotide sequence encoding rat CARK was deposited with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209, on March 21, 2000 and assigned Accession Number PTA-1530. This deposit

will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an admission that a deposit is required under 35 U.S.C. §112.

On page 77, please replace the paragraphs beginning on line 19 with the following:

The sequence of the positive clone was determined and found to contain an open reading frame. The nucleotide sequence encoding the human CARK protein comprises about 3025 nucleic acids, and has the nucleic acid sequence shown in Figures 1A-B and set forth as SEQ ID NO:1. The protein encoded by this nucleic acid comprises about 835 amino acids, and has the amino acid sequence shown in Figures 1A-B and set forth as SEQ ID NO:2.

A clone containing the rat CARK cDNA was also identified. The nucleotide sequence encoding the rat CARK protein comprises about 3026 nucleic acids, and has the nucleic acid sequence shown in Figures 5A-D and set forth as SEQ ID NO:7. The protein encoded by this nucleic acid comprises about 835 amino acids, and has the amino acid sequence shown in Figures 5A-D and set forth as SEQ ID NO:8.

On page 78, please replace the paragraph beginning on line 19 with the following:

The CARK protein was aligned with the A. Thaliana kinase 2 (Accession No.Z97337), A. Thaliana kinase 3 (Accession No. AC003113), Arabidopsis thaliana (Accession No. AL031135), C. elegans kinase (Accession No. AF024491), D. discoideum protein tyrosine kinase (Accession No. A35670), D. discoideum protein tyrosine kinase (Accession No. U01064), H. sapiens serine/threonine kinase (Accession No. Z48615), human raf1 (Accession No. W13107), human Raf1 kinase (Accession No. R98215), and soybean kinase (Accession No. M67449) using the Clustal method with a PAM250 residue weight table. This alignment is shown in Figures 3A-L.

On page 79, please replace the paragraphs beginning on line 20 with the following:

The rat CARK nucleic acid sequence was globally aligned with the human CARK nucleic acid sequence using the GAP program in the GCG software package, using a nwsgapdna matrix a gap weight of 12 and a length weight of 4. The results showed a 82.2% identity between the two sequences (see Figures 7<u>A-F</u>).

The rat CARK protein sequence was globally aligned with the human CARK protein sequence using the GAP program in the GCG software package, using a Blosum 62 matrix and a gap weight of 12 and a length weight of 4. The results showed a 91.4% identity between the two sequences (see Figures 8<u>A-B</u>).